defects that allow fluid to which the surface is exposed to communicate electrically with the surface. In this context, the fluid communicates electrically with the surface by contacting the surface or coming in close enough proximity to the surface that electronic communication via tunneling or the like, can occur.

[0036] The term "biological binding" refers to the interaction between a corresponding pair of molecules that exhibit mutual affinity or binding capacity, typically specific or non-specific binding or interaction, including biochemical, physiological, and/or pharmaceutical interactions. Biological binding defines a type of interaction that occurs between pairs of molecules including proteins, nucleic acids, glycoproteins, carbohydrates, hormones and the like. Specific examples include antibody/antigen, antibody/hapten, enzyme/substrate, enzyme/inhibitor, enzyme/cofactor, binding protein/substrate, carrier protein/substrate, lectin/carbohydrate, receptor/hormone, receptor/effector, complementary strands of nucleic acid, protein/nucleic acid repressor/inducer, ligand/cell surface receptor, virus/ligand, etc.

[0037] The term "binding partner" refers to a molecule that can undergo binding with a particular molecule. Biological binding partners are examples. For example, Protein A is a binding partner of the biological molecule IgG, and vice versa. .

[0038] The term "determining" refers to quantitative or qualitative analysis of a species via, for example, spectroscopy, ellipsometry, piezoelectric measurement, immunoassay, electrochemical measurement, and the like. "Determining" also means detecting or quantifying interaction between species, e.g. detection of binding between two species.

[0039] The term "self-assembled monolayer" (SAM) refers to a relatively ordered assembly of molecules spontaneously chemisorbed on a surface, in which the molecules are oriented approximately parallel to each other and roughly perpendicular to the surface. Each of the molecules includes a functional group that adheres to the surface, and a portion that interacts with neighboring molecules in the monolayer to form the relatively ordered array. See Laibinis, P. E.; Hickman, J.; Wrighton, M. S.; Whitesides, G. M. *Science* 245, 845 (1989), Bain, C.; Evall, J.; Whitesides, G. M. *J. Am. Chem. Soc.* 111, 7155-7164 (1989), Bain, C.; Whitesides, G. M. *J. Am. Chem. Soc.* 111, 7164-7175 (1989), each of which is incorporated herein by reference.

[0040] The term "self-assembled mixed monolayer" refers to a heterogeneous self-assembled monolayer, that is, one made up of a relatively ordered assembly of at least two different molecules.

[0041] The present invention provides techniques, kits, and articles for determination of binding between chemical or biological species, especially for determining which, of a series of species, bind to a particular target species and which do not. Techniques of the invention are useful for determination of essentially any binding interactions, typically biological binding interactions.

[0042] Certain embodiments of the invention make use of self-assembled monolayers (SAMs) on surfaces, such as surfaces of colloid particles, and articles such as colloid particles having surfaces coated with SAMs. In one set of preferred embodiments, SAMs formed completely of synthetic molecules completely cover a surface or a region of a surface, e.g. completely cover the surface of a colloid particle. "Synthetic molecule", in this context, means a molecule that is not naturally occurring, rather, one synthesized under the direction of human or human-created or human-directed control. "Completely cover" in this context, means that there is no portion of the surface or region that directly contacts a protein, antibody, or other species that prevents complete, direct coverage with the SAM. I.e. the surface or region includes, across its entirety, a SAM consisting completely of non-naturally-occurring molecules (i.e. synthetic molecules). The SAM can be made up completely of SAM-forming species that form close-packed SAMs at surfaces, these species in combination with molecular wires or other species able to promote electronic communication through the SAM (including defect-promoting species able to participate in a SAM), other species able to participate in a SAM, and any combination of these. Preferably, all of the species that participate in the SAM include a functionality that binds, optionally covalently, to the surface, such as a thiol which will bind to a gold surface covalently. A self-assembled monolayer on a surface, in accordance with the invention, can be comprised of a mixture of species (e.g. thiol species when gold is the surface) that can present (expose) essentially any chemical or biological functionality. For example, they can include tri-ethylene glycol-terminated species (e.g. tri-ethylene glycol-terminated thiols) to resist non-specific adsorption, and other species (e.g. thiols) terminating in a binding partner of an affinity tag, e.g. terminating in a chelate that can coordinate a metal such as nitrilotriacetic acid which, when in complex with nickel atoms, captures histidine-tagged binding species. These arrangements can be used for a variety of embodiments of the invention. As an example, a self-assembled monolayer, whether formed on a colloid or on another surface, can be comprised of a mixture of thiol species (when gold is the surface) that include triethylene glycol-terminated thiols to resist non-specific adsorption and thiols terminating in a binding partner of an affinity tag, e.g. terminating in a chelate that can coordinate a metal such as nitrilo tri-acetic acid which, when in complex with nickel atoms, capture histidine-tagged binding species. In a preferred embodiment the binding species is a beta-amyloid peptide which can readily self-aggregate. The present invention provides a method for rigorously controlling the concentration of the histidine-tagged peptides presented on the colloid surface. Without this rigorous control over peptide density on each colloid particle, co-immobilized peptides would readily aggregate with each other to form micro-hydrophobic-domains that would catalyze colloid-colloid aggregation in the absence of aggregate-forming species present in a sample. This is an advantage of the present invention, over existing colloid agglutination assays.

[0043] The methods described in the present invention produce self-assembled monolayers on colloids that resist non-specific adsorption without protein blocking steps, such as blocking with BSA. The methods described herein also produce derivatized colloids that are stable in biologically relevant fluids and do not require detergents (for stability; maintaining colloids in suspension), which interfere with binding reactions. This allows sensitive binding assays to be performed in solution. This abrogates the need for having binding partners adhered to adsorbent surfaces, as is common for existing colloid agglutination assays. As is discussed below, detergent can advantageously be used for